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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/801,302	03/07/2001	Patrick F. Kelly	2427/1G685US1	2679

29311 7590 09/23/2003

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EXAMINER	
QIAN, CELINE X	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/801,302	KELLY ET AL.	
	Examiner	Art Unit	
	Celine X Qian	1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 06 August 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *see reasons below.*

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet.*

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *2-18.*

   Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER

Continuation of 5. does NOT place the application in condition for allowance because: it does not overcome the 103 (a) rejection raised in the previous office action mailed on 5/7/03. In response to this rejection, Applicants argue that the combination of the references do not render the claims obvious. Applicants argue that none of references teaches the limitation of the viral particles are substantially free of factors that induce stem cell differentiation by being substantially free of producer cells and producer cell supernatant. Further Applicants argue that Uchida and Rebel references teach away from the claimed invention because they do not teach the use of RD114 pseudotyped vectors, and Rebel stresses the superior properties of VSV-G pseudotyped viral particles. Applicants assert that the retroviral vector particles cannot be efficiently concentrated to higher titers by ultracentrifugation except VSV-G pseudotyped vector, thus the claimed invention demonstrated unexpected results. Finally, Applicants argue that the rejection is based on hindsight reasoning because the prior art do not suggest the desirability of the modification to reach the claimed invention. These arguments have been fully considered but deemed unpersuasive. The detailed teaching and the reasons for obviousness of the invention in view of the prior art were discussed in detail in the previous office action mailed on 5/7/02. Contrary to Applicants' assertion, Hernnemann reference does teach the limitation of substantially free of producer cells and producer cell supernatant. The specification does not define how much supernatant needs to be removed would be considered as "substantially free." In addition, the broadest claim (3) does not recite the step of how the supernatant is removed. As such, filtration of the supernatant through a filter is within the scope of the claim because the filtration step taught by Hernnemann would not only remove the producer cells but also "substantial" amount of supernatant that contains other molecules that would cause stem cell differentiation.

In response to applicant's arguments against the Uchida and Rebel references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Althouth both references do not teach vector particles pseudotyped with RD114, such teaching is provided in Onodera and Porter et al. Porter et al. further provided a clear motivation of using RD114 pseudotyped vector for in vivo human gene therapy (thus transduce stem cell) because this envelope is resistant to the inactivation of human serum (see abstract). Further, Rebel et al. do not teach away from the claimed invention because it only teaches that one day ex vivo culture allows effective gene transfer. Altough Rebel et al. teach the use of VSV-G vector, it does not teach away from using other types of vector system. Similarly, methods such as pre-stimulation, use of fibronectin, and modifying vectors are different ways of improving transduction efficiency which can be used together, but not mutually exclusive. Further, Rebel et al. do not teach that RD114 cannot be concentrated by the method of ultracentrifugation. Therefore, Rebel et al. do not teach away from the claimed invention.

In response to Applicants' argument that the method of concentrating RD114 pseudotyped virus result in unexpected result, Applicants are reminded that such unexpected results is not a limitation in the claim. Unless the claims are amended to include such results, the currently applied references still render the claimed invention obvious. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In this case, the prior art does suggest the motivation for combine as discussed in the previous office action and above. Therefore, the rejection is maintained

Applicants request the withdraw of finality of the previous office action mailed on 5/7/03 on the bases that the rejection is new. Such request is not granted because the new rejection is necessitated by Applicants' amendment. Although claim 3 is presented in the original application, however, the amendment not only incorporate the limitation of claim 1 but also incorporate a new limitation that recites "and whereby the transduced stem cells are capable of expessing the gene of interest and repopulating cell lineages when transplanted into a host." Such limitation was not in the oringinally filed claim 3. Therefore, the new grounds of rejection is necessitated by Applicants' amendment.

Applicants also request the rejoining of claims 19-30 because Applicants allege that the restriction is not proper. As discussed in the previous office action, claims 19-30 are withdrawn from further consideration by the examiner in accordance with 37 CFR 1.142(b) for being directed to non elected subject matter. (See MPEP § 809.02(c) and § 821.01 through § 821.03). If Applicants traverse the finality of the restriction requirement, Applicant may file a petition under 37 CFR 1.144 for review of the restriction requirement. Claims 19-30 will not be rejoined at present .